

AMENDMENTS TO THE CLAIMS (NONE)

1. **(Original)** A lipopeptide comprising a polypeptide conjugated to one or more lipid moieties wherein:

(i) said polypeptide comprises an amino acid sequence that comprises:

(a) the amino acid sequence of a T helper cell (Th) epitope and the amino acid sequence of a cytotoxic T cell (CTL) epitope, wherein said amino acid sequences are different; and

(b) one or more internal lysine residues or internal lysine analog residues for covalent attachment of each of said lipid moieties via the epsilon-amino group or terminal side-chain group of said lysine or lysine analog; and

(ii) each of said one or more lipid moieties is covalently attached to an epsilon-amino group of said one or more internal lysine residues or to a terminal side-chain group of said one or more internal lysine analog residues.

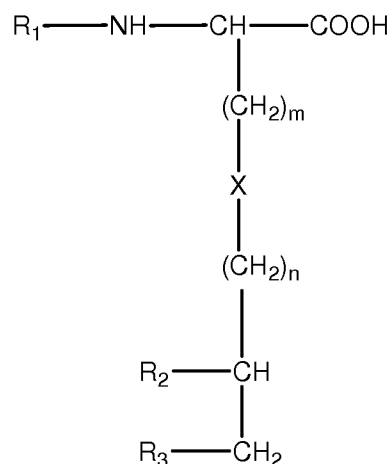
2. **(Original)** The lipopeptide of claim 1 wherein the lipid is attached to the epsilon-amino group of a lysine residue.

3. **(Previously Presented)** The lipopeptide of claim 1 wherein the internal lysine residue to which a lipid moiety is attached is positioned between the Th epitope and the CTL epitope.

4. **(Previously Presented)** The lipopeptide of claim 1 wherein the internal lysine residue to which a lipid moiety is attached is positioned within the Th epitope.

5. **(Previously Presented)** The lipopeptide of claim 1 wherein the lipid moiety has a structure of General Formula (VII):

Formula (VII)



wherein:

- (i) X is selected from the group consisting of sulfur, oxygen, disulfide (-S-S-), and methylene (-CH₂-), and amino (-NH-);
- (ii) m is an integer being 1 or 2;
- (iii) n is an integer from 0 to 5;
- (iv) R₁ is selected from the group consisting of hydrogen, carbonyl (-CO-), and R'-CO- wherein R' is selected from the group consisting of alkyl having 7 to 25 carbon atoms, alkenyl having 7 to 25 carbon atoms, and alkynyl having 7 to 25 carbon atoms, wherein said alkyl, alkenyl or alkynyl group is optionally substituted by a hydroxyl, amino, oxo, acyl, or cycloalkyl group;
- (v) R₂ is selected from the group consisting of R'-CO-O-, R'-O-, R'-O-CO-, R'-NH-CO-, and R'-CO-NH-, wherein R' is selected from the group consisting of alkyl having 7 to 25 carbon atoms, alkenyl having 7 to 25 carbon atoms, and alkynyl having 7 to 25 carbon atoms, wherein said alkyl, alkenyl or alkynyl group is optionally substituted by a hydroxyl, amino, oxo, acyl, or cycloalkyl group; and
- (vi) R₃ is selected from the group consisting of R'-CO-O-, R'-O-, R'-O-CO-,

R'-NH-CO-, and R'-CO-NH-, wherein R' is selected from the group consisting of alkyl having 7 to 25 carbon atoms, alkenyl having 7 to 25 carbon atoms, and alkynyl having 7 to 25 carbon atoms, wherein said alkyl, alkenyl or alkynyl group is optionally substituted by a hydroxyl, amino, oxo, acyl, or cycloalkyl group

and wherein each of R₁, R₂ and R₃ are the same or different.

6. **(Original)** The lipopeptide of claim 5 wherein X is sulfur; m and n are both 1; R₁ is selected from the group consisting of hydrogen, and R'-CO-, wherein R' is an alkyl group having 7 to 25 carbon atoms; and R₂ and R₃ are selected from the group consisting of R'-CO-O-, R'-O-, R'-O-CO-, R'-NH-CO-, and R'-CO-NH-, wherein R' is an alkyl group having 7 to 25 carbon atoms.

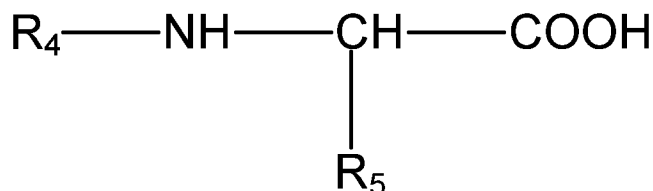
7. **(Original)** The lipopeptide of claim 6 wherein R' is selected from the group consisting of: palmitoyl, myristoyl, stearoyl, lauroyl, octanoyl, decanoyl, and cholesterol.

8. **(Previously Presented)** The lipopeptide of claim 5 wherein the lipid is contained within a lipoamino acid moiety selected from the group consisting of: Pam1Cys, Pam2Cys, Pam3Cys, Chol2Lys, Ste2Cys, Lau2Cys, and Oct2Cys.

9. **(Original)** The lipopeptide according to claim 8 wherein the lipoamino acid moiety is Pam2Cys.

10. **(Previously Presented)** The lipopeptide of claim 1 wherein the lipid moiety has the following General Formula (VIII):

Formula (VIII)



wherein:

- (i) R₄ is selected from the group consisting of: (i) an alpha-acyl-fatty acid residue consisting of between about 7 and about 25 carbon atoms; (ii) an alpha-alkyl-beta-hydroxy-fatty acid residue; (iii) a beta-hydroxy ester of an alpha-alkyl-beta-hydroxy-fatty acid residue; and (iv) a lipoamino acid residue; and
- (ii) R₅ is hydrogen or the side chain of an amino acid residue.

11. **(Previously Presented)** The lipopeptide of claim 1 wherein the lipid moiety is separated from the peptide moiety by a spacer.

12. **(Original)** The lipopeptide of claim 11 wherein the spacer comprises arginine, serine or 6-aminohexanoic acid.

13. **(Previously Presented)** The lipopeptide of claim 11 wherein the spacer consists of a serine homodimer.

14. **(Previously Presented)** The lipopeptide of claim 1 wherein the internal lysine or internal lysine analog is nested within a synthetic amino acid sequence having low immunogenicity.

15. **(Previously Presented)** The lipopeptide of claim 1 wherein the T-helper epitope is a T-helper epitope of influenza virus haemagglutinin or a T-helper epitope of canine distemper virus F (CDV-F) protein.

16. **(Original)** The lipopeptide of claim 15 wherein the T-helper epitope of influenza virus haemagglutinin comprises the amino acid sequence set forth in SEQ ID NO: 1.

17. **(Original)** The lipopeptide of claim 15 wherein the T-helper epitope of CDV-F protein comprises the amino acid sequence set forth in SEQ ID NO: 20.

18. **(Previously Presented)** The lipopeptide of claim 1 wherein the CTL epitope is from an immunogenic protein, lipoprotein, or glycoprotein of a virus.

19. **(Original)** The lipopeptide according to claim 18 wherein the virus is influenza virus.
20. **(Original)** The lipopeptide of claim 19 wherein the CTL epitope comprises the amino acid sequence set forth in SEQ ID NO: 2.
21. **(Original)** The lipopeptide according to claim 18 wherein the virus is hepatitis C virus.
22. **(Original)** The lipopeptide of claim 21 wherein the CTL epitope comprises the amino acid sequence set forth in SEQ ID NO: 176.
23. **(Previously Presented)** The lipopeptide of claim 1 wherein the CTL epitope is from an immunogenic protein, lipoprotein, or glycoprotein of a prokaryotic organism.
24. **(Original)** The lipopeptide according to claim 23 wherein the CTL epitope is from *Listeria monocytogenes*.
25. **(Original)** The lipopeptide of claim 24 wherein the CTL epitope comprises the amino acid sequence set forth in SEQ ID NO: 172.
26. **(Previously Presented)** The lipopeptide of claim 1 wherein the CTL epitope is from an immunogenic protein, lipoprotein, or glycoprotein of a eukaryotic organism.
27. **(Original)** The lipopeptide according claim 26 wherein the eukaryotic organism is a parasite.
28. **(Original)** The lipopeptide according to claim 26 wherein the eukaryotic organism is a mammal.

29. **(Original)** The lipopeptide according to claim 28 wherein the CTL epitope is from an ovalbumin protein of a mammal or a tumor cell.

30. **(Original)** The lipopeptide according to claim 29 wherein the CTL epitope comprises the amino acid sequence set forth in SEQ ID NO: 173.

31. **(Previously Presented)** The lipopeptide of claim 1 wherein the polypeptide comprises an amino acid sequence selected from the group consisting of: SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 174, SEQ ID NO: 175 and SEQ ID NO: 177.

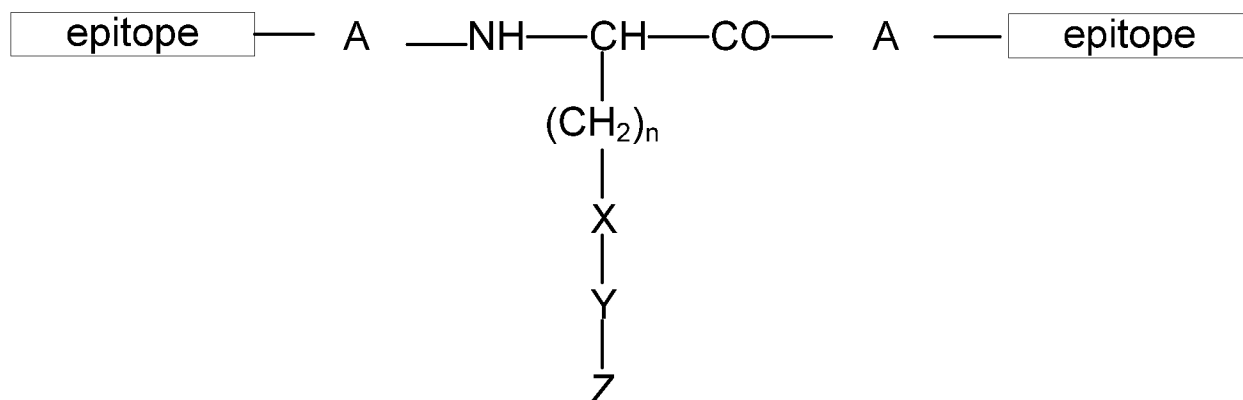
32. **(Previously Presented)** The lipopeptide of claim 1 capable of upregulating the surface expression of MHC class II molecules on immature dendritic cells (DC).

33. **(Original)** The lipopeptide of claim 32 wherein the DC are D1 cells.

34. **(Original)** A lipopeptide comprising a polypeptide conjugated to one or more lipid moieties wherein:

- (i) said polypeptide comprises an amino acid sequence that comprises:
 - (a) the amino acid sequence of a T helper cell (Th) epitope and the amino acid sequence of a CTL epitope, wherein said amino acid sequences are different; and
 - (b) one or more internal lysine or lysine analogue residues for covalent attachment of each of said lipid moieties via the epsilon-amino group of said one or more lysine or lysine analogue residues;
- (ii) each of said one or more lipid moieties is covalently attached to an epsilon-amino group of said one or more internal lysine residues; and
- (iii) said lipopeptide has the general Formula (VI):

Formula (VI):



wherein:

epitope is a T-helper epitope or CTL epitope;

A is either present or absent and consists of an amino acid spacer of about 1 to about 6 amino acids in length;

n is an integer having a value of 1, 2, 3, or 4;

X is a terminal side-chain group selected from the group consisting of NH, O and S;

Y is either present or absent and consists of an amino acid spacer of about 1 to about 6 amino acids in length; and

Z is a lipid moiety.

35. **(Original)** The lipopeptide of claim 34 wherein A is absent.

36. **(Previously Presented)** The lipopeptide of claim 34 wherein Y is present and consists of a serine homodimer.

37. **(Previously Presented)** The lipopeptide of claim 34 wherein Z is selected from the group consisting of: Pam₁Cys, Pam₂Cys, Pam₃Cys, Chol₂Lys, Ste₂Cys, Lau₂Cys, and Oct₂Cys.

38. **(Previously Presented)** The lipopeptide of claim 34 capable of upregulating the surface expression of MHC class II molecules on immature dendritic cells (DC).

39. **(Original)** The lipopeptide of claim 38 wherein the DC are D1 cells.
40. **(WITHDRAWN)** A method of producing a lipopeptide comprising:
- (i) producing a polypeptide comprising an amino acid sequence that comprises:
the amino acid sequence of a T helper cell (Th) epitope and the amino acid sequence of a CTL epitope, wherein said amino acid sequences are different; and
one or more internal lysine residues or internal lysine analog residues; and
 - (ii) covalently attaching each of said one or more lipid moieties directly or indirectly to an epsilon-amino group of said one or more internal lysine residues or to the terminal side-chain group of said one or more internal lysine analog residues so as to produce a lipopeptide having the lipid moiety attached to the epsilon amino group of said internal lysine residue or having the lipid moiety attached to the terminal side-chain group of said internal lysine analog residue.
41. **(WITHDRAWN)** The method of claim 40 wherein the polypeptide is synthesized by a chemical synthesis means.
42. **(WITHDRAWN)** The method of claim 40 further comprising producing the lipid moiety.
43. **(WITHDRAWN)** The method of claim 42 comprising synthesizing the lipid moiety as a lipoamino acid.
44. **(WITHDRAWN)** The method according to claim 43 further comprising adding a spacer to the amino acid moiety of the lipoamino acid.
45. **(WITHDRAWN)** The method according to claim 44 wherein the spacer comprises an arginine homodimer or serine homodimer or 6-aminohexanoic acid .

46. **(WITHDRAWN)** The method of claim 44 comprising adding the spacer to the lipoamino acid via the terminal carboxy group in a process that comprises performing a condensation, addition, substitution, or oxidation reaction.

47. **(WITHDRAWN)** The method of claim 44 wherein the spacer comprises a terminal protected amino acid residue to facilitate conjugation of the lipoamino acid to a polypeptide.

48. **(WITHDRAWN)** The method of claim 47 further comprising de-protecting the terminal protected amino acid of the spacer and conjugating the lipoamino acid to a polypeptide.

49. **(WITHDRAWN)** The method of claim 43 comprising adding a spacer to a non-modified epsilon amino group of the polypeptide in a process comprising performing a nucleophilic substitution reaction.

50. **(WITHDRAWN)** The method of claim 49 wherein the polypeptide has an amino acid sequence comprising a single internal lysine or lysine analog residue and a blocked N-terminus.

51. **(WITHDRAWN)** The method according to claim 49 wherein the spacer comprises an arginine homodimer or serine homodimer or 6-aminohexanoic acid .

52. **(Previously Presented)** A composition comprising the lipopeptide of claim 1 and a pharmaceutically acceptable excipient or diluent.

53. **(Original)** The composition of claim 52 further comprising a biologic response modifier (BRM).

54. **(WITHDRAWN)** A method of eliciting an immune response in a subject comprising administering the lipopeptide of claim 1 to said subject for a time and under

conditions sufficient to elicit a cytotoxic T cell response against a CTL epitope in the lipopeptide.

55. **(WITHDRAWN)** The method according to claim 54 wherein the lipopeptide is administered intranasally to the subject.

56. **(WITHDRAWN)** The method according to claim 54 wherein the lipopeptide is administered to the subject by injection.

57. **(WITHDRAWN)** A method of immunizing a subject against influenza virus comprising administering to said subject a lipopeptide comprising a polypeptide conjugated to one or more lipid moieties, wherein:

- (i) said polypeptide comprises:
 - (a) the amino acid sequence of a T helper cell (Th) epitope and the amino acid sequence of a CTL epitope of an influenza virus protein, and wherein said amino acid sequences are different;
 - (b) one or more internal lysine residues or internal lysine analog residues for covalent attachment of each of said lipid moieties via an epsilon-amino group of said internal lysine or via a terminal side-chain group of said internal lysine analog; and
 - (c) each of said one or more lipid moieties is covalently attached directly or indirectly to an epsilon-amino group of said one or more internal lysine residues or to a terminal side-chain group of said one or more internal lysine analog residues; and
- (ii) said lipopeptide is administered for a time and under conditions sufficient to elicit a CTL response to said CTL epitope.

58. **(WITHDRAWN)** The method of claim 57 wherein the lipopeptide is administered in combination with a pharmaceutically acceptable excipient or diluent.

59. **(WITHDRAWN)** The method of claim 57 wherein immunological memory is generated against the CTL epitope.

60. **(WITHDRAWN)** The method of claim 57 wherein the CTL epitope comprises the amino acid sequence set forth in SEQ ID NO: 2.

61. **(WITHDRAWN)** The method of claim 57 wherein the T-helper epitope comprises an amino acid sequence as set forth in SEQ ID NO: 1 or SEQ ID NO: 20.

62. **(WITHDRAWN)** The method of claim 57 wherein the lipid moiety comprises a lipoamino acid selected from the group consisting of: (i) Pam₁Cys; (ii) Pam₂Cys; (iii) Pam₃Cys; and (iv) Chol₂Lys.

63. **(WITHDRAWN)** The method according to claim 62 wherein the lipid moiety comprises the lipoamino acid Pam₂Cys.

64. **(WITHDRAWN)** The method of claim 57 further comprising producing the lipopeptide.

65. **(WITHDRAWN)** The method of claim 57 further comprising determining the immune response of the subject using a sample taken previously from the subject.

66. **(Previously Presented)** A vaccine against an influenza virus comprising the lipopeptide of claim 1 wherein the CTL epitope is from an influenza virus protein.

67. **(WITHDRAWN)** Use of the lipopeptide according to claim 1 in the preparation of a vaccine against an influenza virus.

68. **(WITHDRAWN)** A method of immunizing a subject against hepatitis C virus comprising administering to said subject a lipopeptide comprising a polypeptide conjugated to one or more lipid moieties, wherein:

- (i) said polypeptide comprises:
 - (a) the amino acid sequence of a T helper cell (Th) epitope and the amino acid sequence of a CTL epitope of a hepatitis C virus protein, and wherein said amino acid sequences are different;
 - (b) one or more internal lysine residues or internal lysine analog residues for covalent attachment of each of said lipid moieties via an epsilon-amino group of said internal lysine or via a terminal side-chain group of said internal lysine analog; and
 - (c) each of said one or more lipid moieties is covalently attached directly or indirectly to an epsilon-amino group of said one or more internal lysine residues or to a terminal side-chain group of said one or more internal lysine analog residues; and
- (ii) said lipopeptide is administered for a time and under conditions sufficient to elicit a CTL response to said CTL epitope.

69. **(WITHDRAWN)** The method of claim 68 wherein the lipopeptide is administered in combination with a pharmaceutically acceptable excipient or diluent.

70. **(WITHDRAWN)** The method of claim 68 wherein immunological memory is generated against the CTL epitope.

71. **(WITHDRAWN)** The method of claim 68 wherein the CTL epitope comprises the amino acid sequence set forth in SEQ ID NO: 176.

72. **(WITHDRAWN)** The method of claim 68 wherein the T-helper epitope comprises an amino acid sequence as set forth in SEQ ID NO: 20.

73. **(WITHDRAWN)** The method of claim 68 wherein the lipid moiety comprises a lipoamino acid selected from the group consisting of: (i) Pam₁Cys; (ii) Pam₂Cys; (iii) Pam₃Cys; and (iv) Chol₂Lys.

74. **(WITHDRAWN)** The method according to claim 73 wherein the lipid moiety comprises the lipoamino acid Pam₂Cys.

75. **(WITHDRAWN)** The method of claim 68 further comprising producing the lipopeptide.

76. **(WITHDRAWN)** The method of claim 68 further comprising determining the immune response of the subject using a sample taken previously from the subject.

77. **(Previously Presented)** A vaccine against a hepatitis C virus comprising the lipopeptide of claim 1 wherein the CTL epitope is from a hepatitis C virus protein.

78. **(WITHDRAWN)** Use of the lipopeptide of claim 1 in the preparation of a vaccine against an hepatitis C virus.

79. **(WITHDRAWN)** A method of immunizing a subject against *Listeria monocytogenes* comprising administering to said subject a lipopeptide comprising a polypeptide conjugated to one or more lipid moieties, wherein:

- (i) said polypeptide comprises:
 - (a) the amino acid sequence of a T helper cell (Th) epitope and the amino acid sequence of a CTL epitope of a *Listeria monocytogenes* protein, and wherein said amino acid sequences are different;
 - (b) one or more internal lysine residues or internal lysine analog residues for covalent attachment of each of said lipid moieties via an epsilon-amino group of said internal lysine or via a terminal side-chain group of said internal lysine analog; and
 - (c) each of said one or more lipid moieties is covalently attached directly or indirectly to an epsilon-amino group of said one or more internal lysine residues or to a terminal side-chain group of said one or more internal lysine analog residues; and

- (ii) said lipopeptide is administered for a time and under conditions sufficient to elicit a CTL response to said CTL epitope.

80. **(WITHDRAWN)** The method of claim 79 wherein the lipopeptide is administered in combination with a pharmaceutically acceptable excipient or diluent.

81. **(WITHDRAWN)** The method of claim 79 wherein immunological memory is generated against the CTL epitope.

82. **(WITHDRAWN)** The method of claim 79 wherein the CTL epitope comprises the amino acid sequence set forth in SEQ ID NO: 172.

83. **(WITHDRAWN)** The method of claim 79 wherein the T-helper epitope comprises an amino acid sequence as set forth in SEQ ID NO: 20.

84. **(WITHDRAWN)** The method of claim 79 wherein the lipid moiety comprises a lipoamino acid selected from the group consisting of: (i) Pam₁Cys; (ii) Pam₂Cys; (iii) Pam₃Cys; and (iv) Chol₂Lys.

85. **(WITHDRAWN)** The method according to claim 84 wherein the lipid moiety comprises the lipoamino acid Pam₂Cys.

86. **(WITHDRAWN)** The method of claim 79 further comprising producing the lipopeptide.

87. **(WITHDRAWN)** The method of claim 79 further comprising determining the immune response of the subject using a sample taken previously from the subject.

88. **(Previously Presented)** A vaccine against *Listeria monocytogenes* comprising the lipopeptide of claim 1 wherein the CTL epitope is from a *Listeria monocytogenes* protein.

89. **(WITHDRAWN)** Use of the lipopeptide of claim 1 in the preparation of a vaccine against *Listeria monocytogenes*.

90. **(WITHDRAWN)** A method of prophylaxis or therapy of cancer comprising administering to said subject a lipopeptide comprising a polypeptide conjugated to one or more lipid moieties, wherein:

- (i) said polypeptide comprises:
 - (a) the amino acid sequence of a T helper cell (Th) epitope and the amino acid sequence of a tumor-specific CTL epitope, wherein said amino acid sequences are different;
 - (b) one or more internal lysine residues or internal lysine analog residues for covalent attachment of each of said lipid moieties via an epsilon-amino group of said internal lysine or via a terminal side-chain group of said internal lysine analog; and
 - (c) each of said one or more lipid moieties is covalently attached directly or indirectly to an epsilon-amino group of said one or more internal lysine residues or to a terminal side-chain group of said one or more internal lysine analog residues; and
- (ii) said lipopeptide is administered for a time and under conditions sufficient to elicit a CTL response to said CTL epitope.

91. **(WITHDRAWN)** The method of claim 90 wherein the lipopeptide is administered in combination with a pharmaceutically acceptable excipient or diluent.

92. **(WITHDRAWN)** The method of claim 90 wherein immunological memory is generated against the CTL epitope.

93. **(WITHDRAWN)** The method of claim 90 wherein the tumor-specific CTL epitope comprises the amino acid sequence set forth in SEQ ID NO: 173.

94. **(WITHDRAWN)** The method of claim 90 wherein the T-helper epitope comprises an amino acid sequence as set forth in SEQ ID NO: 20.

95. **(WITHDRAWN)** The method of claim 90 wherein the lipid moiety comprises a lipoamino acid selected from the group consisting of: (i) Pam₁Cys; (ii) Pam₂Cys; (iii) Pam₃Cys; and (iv) Chol₂Lys.

96. **(WITHDRAWN)** The method according to claim 95 wherein the lipid moiety comprises the lipoamino acid Pam₂Cys.

97. **(WITHDRAWN)** The method of claim 90 further comprising producing the lipopeptide.

98. **(WITHDRAWN)** The method of claim 90 further comprising determining the immune response of the subject using a sample taken previously from the subject.

99. **(Previously Presented)** A prophylactic or therapeutic vaccine against cancer comprising the lipopeptide of claim 1 wherein the CTL epitope is a tumor-specific CTL epitope.

100. **(WITHDRAWN)** Use of the lipopeptide of claim 1 in the preparation of a prophylactic or therapeutic vaccine against cancer.